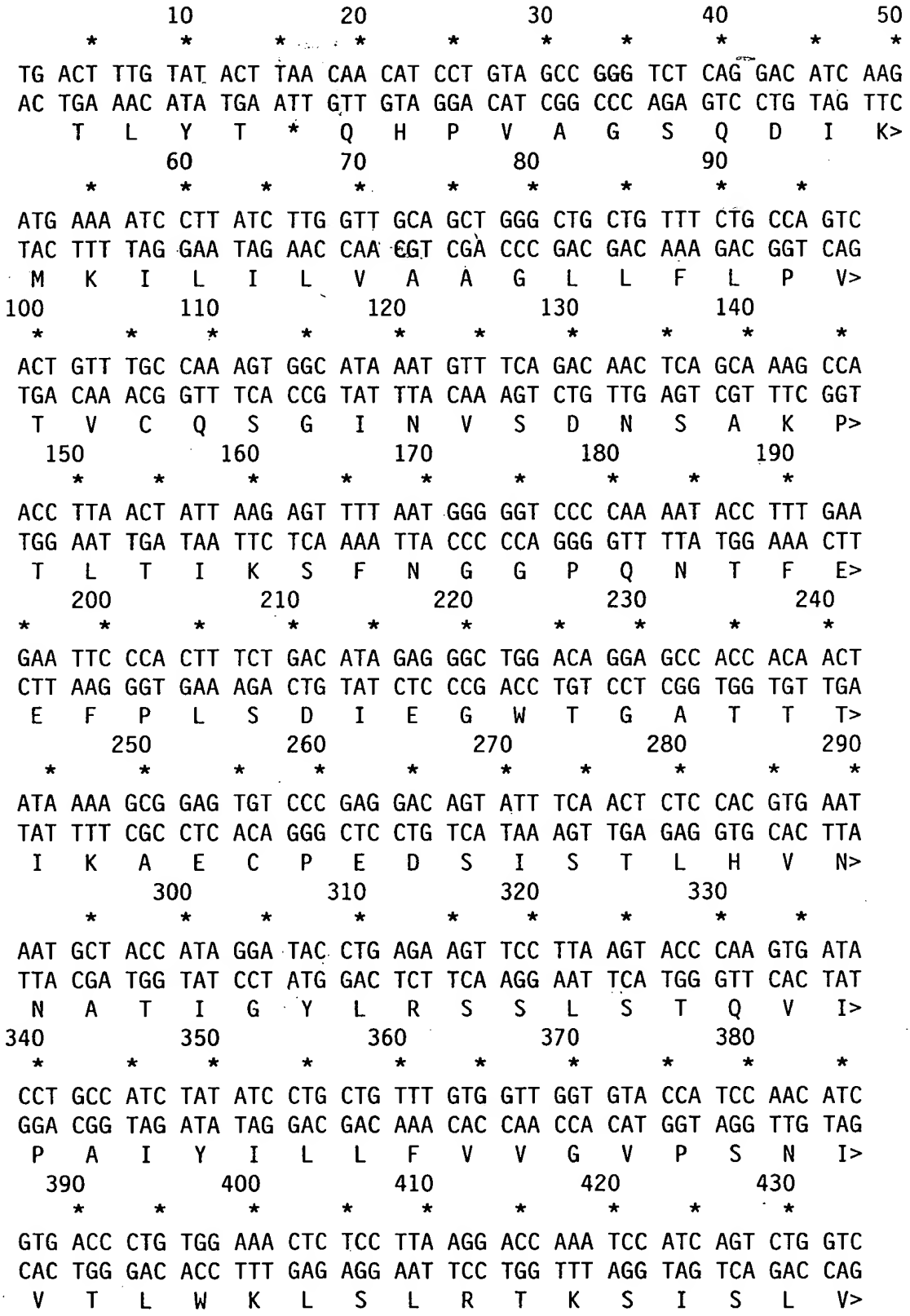
FIG. 1-1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TG ACT TTG TAT ACT TAA CAA CAT CCT GTA GCC GGG TCT CAG GAC ATC AAG
AC TGA AAC ATA TGA ATT GTT GTA GGA CAT CGG CCC AGA GTC CTG TAG TTC
T L Y T * Q H P V A G S Q D I K>
60 70 80 90
ATG AAA ATC CTT ATC TTG GTT GCA GCT GGG CTG CTG TTT CTG CCA GTC
TAC TTT TAG GAA TAG AAC CAA CGT CGA CCC GAC GAC AAA GAC GGT CAG
M K I L I L V A A G L L F L P V>
100 110 120 130 140
ACT GTT TGC CAA AGT GGC ATA AAT GTT TCA GAC AAC TCA GCA AAG CCA
TGA CAA ACG GTT TCA CCG TAT TTA CAA AGT CTG TTG AGT CGT TTC GGT
T V C Q S G I N V S D N S A K P>
150 160 170 180 190
ACC TTA ACT ATT AAG AGT TTT AAT GGG GGT CCC CAA AAT ACC TTT GAA
TGG AAT TGA TAA TTC TCA AAA TTA CCC CCA GGG GTT TTA TGG AAA CTT
T L T I K S F N G G P Q N T F E>
200 210 220 230 240
GAA TTC CCA CTT TCT GAC ATA GAG GGC TGG ACA GGA GCC ACC ACA ACT
CTT AAG GGT GAA AGA CTG TAT CTC CCG ACC TGT CCT CGG TGG TGT TGA
E F P L S D I E G W T G A T T T>
250 260 270 280 290
ATA AAA GCG GAG TGT CCC GAG GAC AGT ATT TCA ACT CTC CAC GTG AAT
TAT TTT CGC CTC ACA GGG CTC CTG TCA TAA AGT TGA GAG GTG CAC TTA
I K A E C P E D S I S T L H V N>
300 310 320 330
AAT GCT ACC ATA GGA TAC CTG AGA AGT TCC TTA AGT ACC CAA GTG ATA
TTA CGA TGG TAT CCT ATG GAC TCT TCA AGG AAT TCA TGG GTT CAC TAT
N A T I G Y L R S S L S T Q V I>
340 350 360 370 380
CCT GCC ATC TAT ATC CTG CTG TTT GTG GTT GGT GTA CCA TCC AAC ATC
GGA CGG TAG ATA TAG GAC GAC AAA CAC CAA CCA CAT GGT AGG TTG TAG
P A I Y I L L F V V G V P S N I>
390 400 410 420 430
GTG ACC CTG TGG AAA CTC TCC TTA AGG ACC AAA TCC ATC AGT CTG GTC
CAC TGG GAC ACC TTT GAG AGG AAT TCC TGG TTT AGG TAG TCA GAC CAG
V T L W K L S L R T K S I S L V>
* * * * * * * * * *

FIG. 1-2

```
    440           450           460           470           480
*     *     *     *     *     *     *     *     *     *     *
ATC TTT CAC ACC AAC CTG GCC ATC GCA GAT CTC CTT TTC TGT GTC ACA
TAG AAA GTG TGG TTG GAC CGG TAG CGT CTA GAG GAA AAG ACA CAG TGT
 I   F   H   T   M   L   A   I   A   D   L   L   F   C   V   T>
      490           500           510           520           530
  *     *     *     *     *     *     *     *     *     *     *
CTG CCA TTT AAG ATC GCC TAC CAT CTC AAT GGC AAC AAC TGG GTA TTT
GAC GGT AAA TTC TAG CGG ATG GTA GAG TTA CCG TTG TTG ACC CAT AAA
 L   P   F   K   I   A   Y   H   L   N   G   N   N   W   V   F>
          540           550           560           570
      *     *     *     *     *     *     *     *     *
GGC GAG GTC ATG TGC CGG ATC ACC ACG GTC GTT TTC TAC GGC AAC ATG
CCG CTC CAG TAC ACG GCC TAG TGG TGC CAG CAA AAG ATG CCG TTG TAC
 G   E   V   M   C   R   I   T   T   V   V   F   Y   G   N   M>
580           590           600           610           620
 *     *     *     *     *     *     *     *     *     *     *
TAC TGC GCT ATC CTG ATC CTC ACT TGC ATG GGC ATC AAC CGC TAC CTG
ATG ACG CGA TAG GAC TAG GAG TGA ACG TAC CCG TAG TTG GCG ATG GAC
 Y   C   A   I   L   I   L   T   C   M   G   I   N   R   Y   L>
  630           640           650           660           670
     *     *     *     *     *     *     *     *     *     *
GCC ACG GCT CAC CCT TTC ACA TAC CAG AAG CTG CCC AAA CGC AGC TTC
CGG TGC CGA GTG GGA AAG TGT ATG GTC TTC GAC GGG TTT GCG TCG AAG
 A   T   A   H   P   F   T   Y   Q   K   L   P   K   R   S   F>
    680           690           700           710           720
*     *     *     *     *     *     *     *     *     *     *
TCC TTG CTC ATG TGT GGC ATA GTG TGG GTC ATG GTT TTC TTA TAC ATG
AGG AAC GAG TAC ACA CCG TAT CAC ACC CAG TAC CAA AAG AAT ATG TAC
 S   L   L   M   C   G   I   V   W   V   M   V   F   L   Y   M>
      730           740           750           760           770
  *     *     *     *     *     *     *     *     *     *     *
CTG CCC TTT GTC ATC CTG AAG CAG GAG TAC CAC CTC GTC CAC TCA GAG
GAC GGG AAA CAG TAG GAC TTC GTC CTC ATG GTG GAG CAG GTG AGT CTC
 L   P   F   V   I   L   K   Q   E   Y   H   L   V   H   S   E>
          780           790           800           810
      *     *     *     *     *     *     *     *     *
ATC ACC ACC TGC CAC GAT GTC GTC GAC GCG TGC GAG TCC CCA TCA TCC
TAG TGG TGG ACG GTG CTA CAG CAG CTG CGC ACG CTC AGG GGT AGT AGG
 I   T   T   C   H   D   V   V   D   A   C   E   S   P   S   S>
820           830           840           850           860
 *     *     *     *     *     *     *     *     *     *     *
TTC CGA TTC TAC TAC TTC GTC TCC TTA GCA TTC TTT GGG TTC CTC ATC
AAG GCT AAG ATG ATG AAG CAG AGG AAT CGT AAG AAA CCC AAG GAG TAG
 F   R   F   Y   Y   F   V   S   L   A   F   F   G   F   L   I>
```

FIG. 1-3

```
  870          880          890          900          910
    *     *      *      *     *      *      *     *      *
CCG TTT GTG ATC ATC ATC TTC TGT TAC ACG ACT CTC ATC CAC AAA CTT
GGC AAA CAC TAG TAG TAG AAG ACA ATG TGC TGA GAG TAG GTG TTT GAA
 P   F   V   I   I   I   F   C   Y   T   T   L   I   H   K   L>
    920          930          940          950          960
*     *      *      *     *      *      *     *      *      *
AAA TCA AAG GAT CGG ATA TGG CTG GGC TAC ATC AAG GCC GTC CTC CTC
TTT AGT TTC CTA GCC TAT ACC GAC CCG ATG TAG TTC CGG CAG GAG GAG
 K   S   K   D   R   I   W   L   G   Y   I   K   A   V   L   L>
       970          980          990          1000         1010
  *      *      *     *      *      *     *      *      *     *
ATC CTT GTG ATT TTC ACA ATT TGC TTT GCC CCC ACC AAC ATC ATA CTC
TAG GAA CAC TAA AAG TGT TAA ACG AAA CGG GGG TGG TTG TAG TAT GAG
 I   L   V   I   F   T   I   C   F   A   P   T   N   I   I   L>
         1020         1030         1040         1050
     *      *     *      *     *      *      *     *     *
GTA ATC CAC CAT GCC AAC TAC TAC TAC CAC AAT ACC GAC AGC TTG TAC
CAT TAG GTG GTA CGG TTG ATG ATG ATG GTG TTA TGG CTG TCG AAC ATG
 V   I   H   H   A   N   Y   Y   Y   H   N   T   D   S   L   Y>
1060         1070         1080         1090         1100
  *      *     *      *     *      *      *     *     *      *
TTT ATG TAT CTT ATT GCT CTG TGC CTG GGG AGC CTG AAT AGC TGC CTA
AAA TAC ATA GAA TAA CGA GAC ACG GAC CCC TCG GAC TTA TCG ACG GAT
 F   M   Y   L   I   A   L   C   L   G   S   L   N   S   C   L>
 1100         1120         1130         1140         1150
    *     *      *      *     *      *      *     *      *
GAT CCA TTC CTT TAC TTT GTC ATG TCG AAA GTT GTA GAT CAG CTT AAT
CTA GGT AAG GAA ATG AAA CAG TAC AGC TTT CAA CAT CTA GTC GAA TTA
 D   P   F   L   Y   F   V   M   S   K   V   V   D   Q   L   N>
   1160         1170         1180         1190         1200
*     *      *      *     *      *      *     *      *      *
CCT TAG TCG GCA ATG GCA AGA CCA CTT TAG AGA CCA AGG AGA GAT ATC
GGA ATC AGC CGT TAC CGT TCT GGT GAA ATC TCT GGT TCC TCT CTA TAG
 P   *   S   A   M   A   R   P   L   *   R   P   R   R   D   I>
       1210         1220
  *      *      *     *
TGG GAA GAC ATA CAT GCT TGG C
ACC CTT CTG TAT GTA CGA ACC G
 W   E   D   I   H   A   W   X>
```

FIG. 2-1

```
        10         20         30         40         50
    *   *   *   *   *   *   *   *   *   *
CCATATGCTA ATATTTCCTT TCAATTACAG GCATAAATGT TTCAGACAAC

        60         70         80         90        100
    *   *   *   *   *   *   *   *   *   *
TCAGCAAAGC CAACCTTAAC TATTAAGAGT TTTAATGGGG GTCCCCAAAA

       110        120        130        140        150
    *   *   *   *   *   *   *   *   *   *
TACCTTTGAA GAATTC---- ---TACAACT CTCCATGTGA ATAATGCTAC

       160        170        180        190        200
    *   *   *   *   *   *   *   *   *   *
CATGGGATAC CTGAGAAGTT CCTTAAGTAC CAAAGTGATA CCTGCCATCT

       210        220        230        240        250
    *   *   *   *   *   *   *   *   *   *
ACATCCTGGT GTTTGTGATT GGTGTACCAG CGAACATCGT GACCCTGTGG

       260        270        280        290        300
    *   *   *   *   *   *   *   *   *   *
AAACTCTCCT CAAGGACCAA ATCCATCTGT CTGGTCATCT TTCACACCAA

       310        320        330        340        350
    *   *   *   *   *   *   *   *   *   *
CCTGGCCATC GCGGATCTCC TTTTCTGTGT CACGCTGCCG TTTAAGATC-

       360        370        380        390        400
    *   *   *   *   *   *   *   *   *   *
-CCTACCATC TCAATGGCAA CAACTGGGTA TTTGGCGAGG TCATGTGCCG

       410        420        430        440        450
    *   *   *   *   *   *   *   *   *   *
GATCACCACG GTCGTTTTCT ACGGCAACAT GTACTGCGCT A---TCCTGA

       460        470        480        490        500
    *   *   *   *   *   *   *   *   *   *
TCCTCACCTG CATGGGCATC AACCGCTACC TGGCCACGGC TCACCCTTTC

       510        520        530        540        550
    *   *   *   *   *   *   *   *   *   *
ACATACCAGA AGCTGCCCAA ACGCAGCTTC TCCATGCTCA TGTGTGGCAT

       560        570        580        590        600
    *   *   *   *   *   *   *   *   *   *
GGTGTGGGTC ATGGTTTTCT TATACATGCT GCCCTTTGTC ATCC---AAG

       610        620        630        640        650
    *   *   *   *   *   *   *   *   *   *
CAGGAGTACC ACCTCGTCCA CTCCGAGATC ACCACCTGCC ACGATGTCGT
```

FIG. 2-2

```
      660        670        680        690        700
    *   *      *   *      *   *      *   *      *   *
CGACGCGTGC GANTCCCCAT CATCCTTCCG ATTCTACTAC TTCGTCTCCT
      710        720        730        740        750
    *   *      *   *      *   *      *   *      *   *
TAGCATTCTT TGGGTTCCTC ATCCCGTTTG TGATCATCAT CTTCTGTTAC
      760        770        780        790        800
    *   *      *   *      *   *      *   *      *   *
ACGACTCTCA TCCACAAACT TAAATCAAAA GATCNGATAT GGCTGGGCTA
      810        820        830        840        850
    *   *      *   *      *   *      *   *      *   *
CATCAAGGCC GTCCTCCTCA TCCTTGTGAA TTTCACCATC TGCTTCCCCC
      860        870        880        890        900
    *   *      *   *      *   *      *   *      *   *
CCACCAAG-- ----GATATC TGGGAAGACG TACATGCTTG GCTGACTTGT
      910        920        930        940        950
    *   *      *   *      *   *      *   *      *   *
GCATGGCACC ATCAGCTCAA TTTTTAATTT TTTAATTTTA ATTTAATTTA
      960        970        980        990       1000
    *   *      *   *      *   *      *   *      *   *
ATTTTATGTT TTTGAGACAG AGCCTCACTG TGTAGTCCTG GCTGGCCTGG
     1010       1020       1030       1040       1050
    *   *      *   *      *   *      *   *      *   *
CTGGTTCTCT ATTTAGACCA GGTTAGCCTT GAACTCACAG AGATCTGCCT
     1060       1070       1080       1090       1100
    *   *      *   *      *   *      *   *      *   *
GCTTCTGCCT CCCAAGTGCT GGGTTCAACC AGGTCTGGCA AGCGCTCCAT
     1110       1120
    *   *      *   *
TTTTCAGCTC CTCTGCAACA GTGC
```

FIG. 3-1

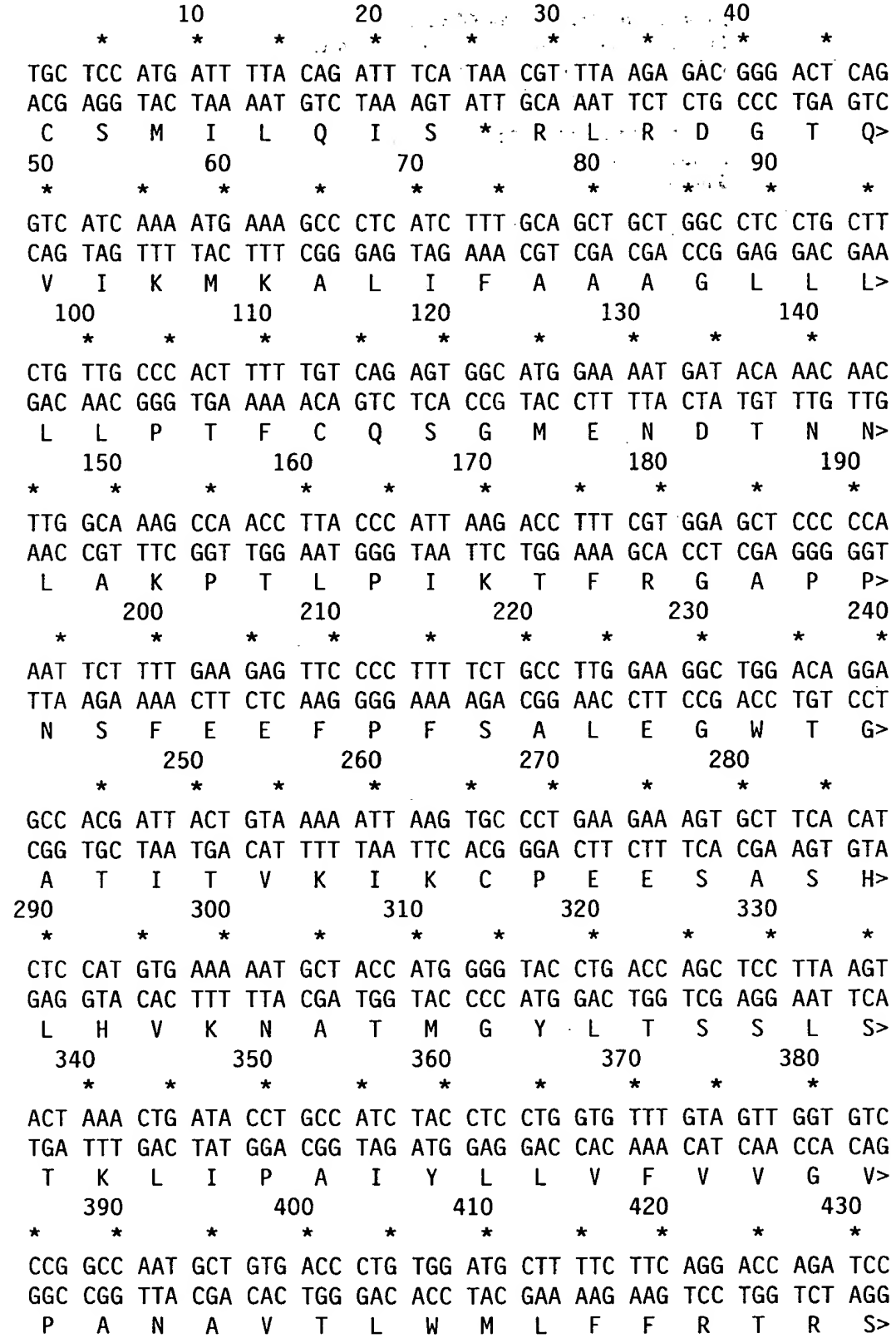

10 20 30 40
TGC TCC ATG ATT TTA CAG ATT TCA TAA CGT TTA AGA GAC GGG ACT CAG
ACG AGG TAC TAA AAT GTC TAA AGT ATT GCA AAT TCT CTG CCC TGA GTC
C S M I L Q I S * R L R D G T Q>
50 60 70 80 90
GTC ATC AAA ATG AAA GCC CTC ATC TTT GCA GCT GCT GGC CTC CTG CTT
CAG TAG TTT TAC TTT CGG GAG TAG AAA CGT CGA CGA CCG GAG GAC GAA
V I K M K A L I F A A A G L L L>
100 110 120 130 140
CTG TTG CCC ACT TTT TGT CAG AGT GGC ATG GAA AAT GAT ACA AAC AAC
GAC AAC GGG TGA AAA ACA GTC TCA CCG TAC CTT TTA CTA TGT TTG TTG
L L P T F C Q S G M E N D T N N>
150 160 170 180 190
TTG GCA AAG CCA ACC TTA CCC ATT AAG ACC TTT CGT GGA GCT CCC CCA
AAC CGT TTC GGT TGG AAT GGG TAA TTC TGG AAA GCA CCT CGA GGG GGT
L A K P T L P I K T F R G A P P>
200 210 220 230 240
AAT TCT TTT GAA GAG TTC CCC TTT TCT GCC TTG GAA GGC TGG ACA GGA
TTA AGA AAA CTT CTC AAG GGG AAA AGA CGG AAC CTT CCG ACC TGT CCT
N S F E E F P F S A L E G W T G>
250 260 270 280
GCC ACG ATT ACT GTA AAA ATT AAG TGC CCT GAA GAA AGT GCT TCA CAT
CGG TGC TAA TGA CAT TTT TAA TTC ACG GGA CTT CTT TCA CGA AGT GTA
A T I T V K I K C P E E S A S H>
290 300 310 320 330
CTC CAT GTG AAA AAT GCT ACC ATG GGG TAC CTG ACC AGC TCC TTA AGT
GAG GTA CAC TTT TTA CGA TGG TAC CCC ATG GAC TGG TCG AGG AAT TCA
L H V K N A T M G Y L T S S L S>
340 350 360 370 380
ACT AAA CTG ATA CCT GCC ATC TAC CTC CTG GTG TTT GTA GTT GGT GTC
TGA TTT GAC TAT GGA CGG TAG ATG GAG GAC CAC AAA CAT CAA CCA CAG
T K L I P A I Y L L V F V V G V>
390 400 410 420 430
CCG GCC AAT GCT GTG ACC CTG TGG ATG CTT TTC TTC AGG ACC AGA TCC
GGC CGG TTA CGA CAC TGG GAC ACC TAC GAA AAG AAG TCC TGG TCT AGG
P A N A V T L W M L F F R T R S>
5'-GGCACGATTACTGTAAAATTAAGTGCCCTGAAGAAAGTGCTTCACAT-3'
3'-CCGTGCTAATGACATTTTTAATTCACGGGACTTCTTTCACGAAGTGTA-5'

FIG. 3-3

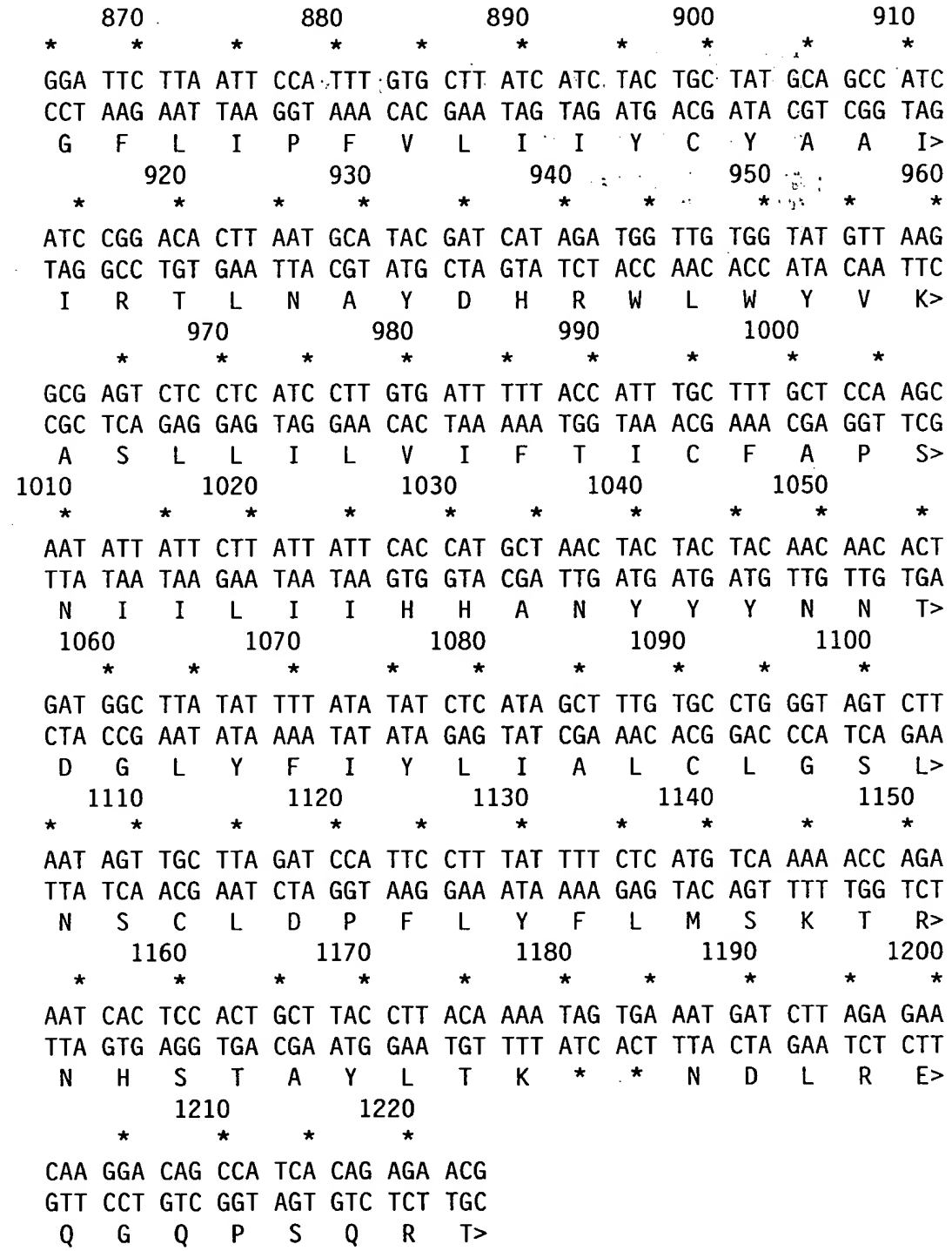

870 880 890 900 910
GGA TTC TTA ATT CCA TTT GTG CTT ATC ATC TAC TGC TAT GCA GCC ATC
CCT AAG AAT TAA GGT AAA CAC GAA TAG TAG ATG ACG ATA CGT CGG TAG
G F L I P F V L I I Y C Y A A I>
920 930 940 950 960
ATC CGG ACA CTT AAT GCA TAC GAT CAT AGA TGG TTG TGG TAT GTT AAG
TAG GCC TGT GAA TTA CGT ATG CTA GTA TCT ACC AAC ACC ATA CAA TTC
I R T L N A Y D H R W L W Y V K>
970 980 990 1000
GCG AGT CTC CTC ATC CTT GTG ATT TTT ACC ATT TGC TTT GCT CCA AGC
CGC TCA GAG GAG TAG GAA CAC TAA AAA TGG TAA ACG AAA CGA GGT TCG
A S L L I L V I F T I C F A P S>
1010 1020 1030 1040 1050
AAT ATT ATT CTT ATT ATT CAC CAT GCT AAC TAC TAC TAC AAC AAC ACT
TTA TAA TAA GAA TAA TAA GTG GTA CGA TTG ATG ATG ATG TTG TTG TGA
N I I L I I H H A N Y Y Y N N T>
1060 1070 1080 1090 1100
GAT GGC TTA TAT TTT ATA TAT CTC ATA GCT TTG TGC CTG GGT AGT CTT
CTA CCG AAT ATA AAA TAT ATA GAG TAT CGA AAC ACG GAC CCA TCA GAA
D G L Y F I Y L I A L C L G S L>
1110 1120 1130 1140 1150
AAT AGT TGC TTA GAT CCA TTC CTT TAT TTT CTC ATG TCA AAA ACC AGA
TTA TCA ACG AAT CTA GGT AAG GAA ATA AAA GAG TAC AGT TTT TGG TCT
N S C L D P F L Y F L M S K T R>
1160 1170 1180 1190 1200
AAT CAC TCC ACT GCT TAC CTT ACA AAA TAG TGA AAT GAT CTT AGA GAA
TTA GTG AGG TGA CGA ATG GAA TGT TTT ATC ACT TTA CTA GAA TCT CTT
N H S T A Y L T K * * N D L R E>
1210 1220
CAA GGA CAG CCA TCA CAG AGA ACG
GTT CCT GTC GGT AGT GTC TCT TGC
Q G Q P S Q R T>

FIG. 3-2

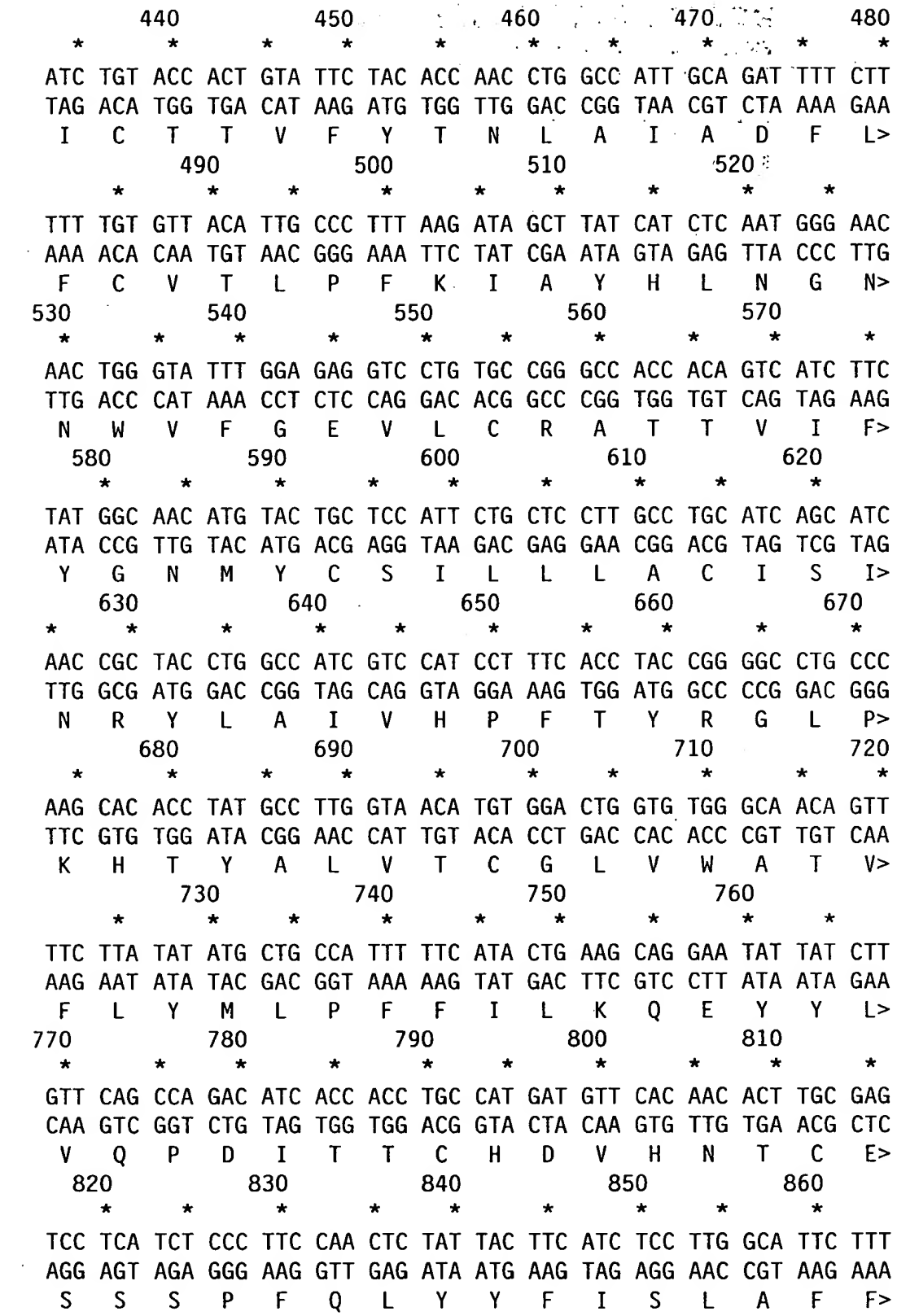

440 450 460 470 480
ATC TGT ACC ACT GTA TTC TAC ACC AAC CTG GCC ATT GCA GAT TTT CTT
TAG ACA TGG TGA CAT AAG ATG TGG TTG GAC CGG TAA CGT CTA AAA GAA
I C T T V F Y T N L A I A D F L>
490 500 510 520
TTT TGT GTT ACA TTG CCC TTT AAG ATA GCT TAT CAT CTC AAT GGG AAC
AAA ACA CAA TGT AAC GGG AAA TTC TAT CGA ATA GTA GAG TTA CCC TTG
F C V T L P F K I A Y H L N G N>
530 540 550 560 570
AAC TGG GTA TTT GGA GAG GTC CTG TGC CGG GCC ACC ACA GTC ATC TTC
TTG ACC CAT AAA CCT CTC CAG GAC ACG GCC CGG TGG TGT CAG TAG AAG
N W V F G E V L C R A T T V I F>
580 590 600 610 620
TAT GGC AAC ATG TAC TGC TCC ATT CTG CTC CTT GCC TGC ATC AGC ATC
ATA CCG TTG TAC ATG ACG AGG TAA GAC GAG GAA CGG ACG TAG TCG TAG
Y G N M Y C S I L L L A C I S I>
630 640 650 660 670
AAC CGC TAC CTG GCC ATC GTC CAT CCT TTC ACC TAC CGG GGC CTG CCC
TTG GCG ATG GAC CGG TAG CAG GTA GGA AAG TGG ATG GCC CCG GAC GGG
N R Y L A I V H P F T Y R G L P>
680 690 700 710 720
AAG CAC ACC TAT GCC TTG GTA ACA TGT GGA CTG GTG TGG GCA ACA GTT
TTC GTG TGG ATA CGG AAC CAT TGT ACA CCT GAC CAC ACC CGT TGT CAA
K H T Y A L V T C G L V W A T V>
730 740 750 760
TTC TTA TAT ATG CTG CCA TTT TTC ATA CTG AAG CAG GAA TAT TAT CTT
AAG AAT ATA TAC GAC GGT AAA AAG TAT GAC TTC GTC CTT ATA ATA GAA
F L Y M L P F F I L K Q E Y Y L>
770 780 790 800 810
GTT CAG CCA GAC ATC ACC ACC TGC CAT GAT GTT CAC AAC ACT TGC GAG
CAA GTC GGT CTG TAG TGG TGG ACG GTA CTA CAA GTG TTG TGA ACG CTC
V Q P D I T T C H D V H N T C E>
820 830 840 850 860
TCC TCA TCT CCC TTC CAA CTC TAT TAC TTC ATC TCC TTG GCA TTC TTT
AGG AGT AGA GGG AAG GTT GAG ATA ATG AAG TAG AGG AAC CGT AAG AAA
S S S P F Q L Y Y F I S L A F F>
440 450 460 470 480

FIG. 4-1

```
       10         20         30         40         50
   *   *   *   *   *   *   *   *   *   *
-ACAGGCATG GAAAATGATA CAAACAACTT GGCAAAGCCA ACCTTACCCA

       60         70         80         90        100
   *   *   *   *   *   *   *   *   *   *
TTAAGACCTT TCGTGGAGCT CCCCCAAATT CTTTTGAAGA GTTCCCCTTT

      110        120        130        140        150
   *   *   *   *   *   *   *   *   *   *
TCTGCCTTGG AAGGCTGGAC AGGAGCCACG ATTACTGTAA AAATTAAGTG

      160        170        180        190        200
   *   *   *   *   *   *   *   *   *   *
CCCTGAAGAA AGTGCTTCAC ATCTCCATGT GAAAAATGCT ACCATGGGGT

      210        220        230        240        250
   *   *   *   *   *   *   *   *   *   *
ACCTGACCAG CTCCTTAAGT ACTAAACTGA TACCTGCCAT CTACCTCCTG

      260        270        280        290        300
   *   *   *   *   *   *   *   *   *   *
GTGTTTGTAG TTGGTGTCCC GGCCAATGCT GTGACCCTGT GGATGCTTTT

      310        320        330        340        350
   *   *   *   *   *   *   *   *   *   *
CTTCAGGACC AGATCCATCT GTACCACTGT ATTCTACACC AACCTGGCCA

      360        370        380        390        400
   *   *   *   *   *   *   *   *   *   *
TTGCAGATTT TCTTTTTTGT GTTACATTGC CCTTTAAGAT AGCTTATCAT

      410        420        430        440        450
   *   *   *   *   *   *   *   *   *   *
CTCAATGGGA ACAACTGGGT ATTTGGAGAG GTCCTGTGCC GGGCCACCAC

      460        470        480        490        500
   *   *   *   *   *   *   *   *   *   *
AGTCATCTTC TATGGCAACA TGTACTGCTC CATTCTGCTC CTTGCCTGCA

      510        520        530        540        550
   *   *   *   *   *   *   *   *   *   *
TCAGCATCAA CCGCTACCTG GCCATCGTCC ATCCTTTCAC CTACCGGGGC

      560        570        580        590        600
   *   *   *   *   *   *   *   *   *   *
CTGCCCAAGC ACACCTATGC CTTGGTAACA TGTGGACTGG TGTGGGCAAC

      610        620        630        640        650
   *   *   *   *   *   *   *   *   *   *
AGTTTTCTTA TATATGCTGC CATTTTTCAT ACTGAAGCAG GAATATTATC
```

FIG. 4-2

```
      660        670        680        690        700
    *   *      *   *      *   *      *   *      *   *
TTGTTCAGCC AGACATCACC ACCTGCCATG ATGTTCACAA CACTTGCGAG

      710        720        730        740        750
    *   *      *   *      *   *      *   *      *   *
TCCTCATCTC CCTTCCAACT CTATTACTTC ATCTCCTTGG CATTCTTTGG

      760        770        780        790        800
    *   *      *   *      *   *      *   *      *   *
ATTCTTAATT CCATTTGTGC TTATCATCTA CTGCTATGCA GCCATCATCC

      810        820        830        840        850
    *   *      *   *      *   *      *   *      *   *
GGACACTTAA TGCATACGAT CATAGATGGT TGTGGTATGT TAAGGCGAGT

      860        870        880        890        900
    *   *      *   *      *   *      *   *      *   *
CTCCTCATCC TTGTGATTTT TACCATTTGC TTTGCTCCAA GCAATATTAT

      910        920        930        940        950
    *   *      *   *      *   *      *   *      *   *
TCTTATTATT CACCATGCTA ACTACTACTA CAACAACACT GATGGCTTAT

      960        970        980        990       1000
    *   *      *   *      *   *      *   *      *   *
ATTTTATATA TCTCATAGCT TTGTGCCTGG GTAGTCTTAA TAGTTGCTTA

     1010       1020       1030       1040       1050
    *   *      *   *      *   *      *   *      *   *
GATCCATTCC TTTATTTTCT CATGTCAAAA ACCAGAAATC ACTCCACTGC

     1060       1070       1080       1090       1100
    *   *      *   *      *   *      *   *      *   *
TTACCTTACA AAATAGTGAA ATGATCTTAG AGAACAAGGA CAGCCATCAC

AGA
```

FIG. 5A

```
hPAR3-1 MKA   LIFAAAGLLLLLP TFCQSGMENDTNNLAKP TLPIK/TFRGAPPN SFEEFPFSALEGWTGATITVKIKC     PEESASHLHVKNATMG
hPAR1-1 MGPRR LLLVAACFSLCGP LLSARTRARRPESKATNATLDPR/SFLLRNPNDKYEPFWEDEEKNESGLTEYRLVSINKSSPLQKQLPAFISEDASG
hPAR2-1 MRSPSAAWLLGAAILLA ASLSCSGTIQG      TNRSSKGR/SLIGKVDGTSHVTGKGVTV                               ETVFSVDEFSAS

                 |---------TM1---------|          |----------TM2---------|                           |---------TM3----------|
hPAR3-87 YLTSSLSTKLIPAIYLLVFVVGVPANAVTLWMLFFRTR SICTTVFYTNLAIADFLFCVTLPFKIAYHLNGNNWVFGEVLCRATTVIFYGNMYCSILLLACISINRYLAI
hPAR1-95 YLTSSWLTLFVPSVYTGVFVVSLPLNIMAIVVFILKMKVKKPAVVYMLHLATADVLFVSVLPFKISYYFSGSDWQFGSELCRFVTAAFYCNMYASILLMTVISIDRFLAV
hPAR2-68 VLTGKLTTVFLPIVYTIVFVVGLPSNGMALWVFLFRTKKKHPAVIYMANLALADLLSVIWFPLKIAYHIHGNNWIYGEALCNVLIGFFYGNMYCSILFMTCLSVQRYWVI

                     |----------TM4----------|                                       |----------TM5-----------|
hPAR3-196 VHPFTYRGLPKHTYALVTCGLVWATVFLYMLPFFILKQEYYLVQPDITTCHDVHNTCESSSPFQLYYFISLAFFGFLIPFVLIIYCYAAIIRTLNA      YDHRWLWYV
hPAR1-205 VYPMQSLSWRTLGRASFTCLAIWALAIAGVVPLVLKEQTIQVPGLNITTCHDVLNETLLEG YYAYYFSAFSAVFFFVPLIISTVCYCSIIRCLSSSAVANRSKK  SRAL
hPAR2-178 VNPMGHSRKKANIAIGI SLAIWLLILLVTIPLYVVKQTIFIPALNITTCHDVLPEQLLVGD MFNYFLSLAIGVFLFPAFLTASAYVLMIRMLRSSAMDENSEKKRKRAI

          |----------TM6--------|             |-------------TM7--------|
hPAR3-301 KASLLILVIFTICFAPSNIILIIHHANYYYNNT DGLYFIYLIALCLGSLNSCLDPFLYFLMSKTRNHSTAYLTK
hPAR1-313 FLSAAVFCIFIICFGPTNVLLIAHYSFLSHTSTTEAAYFAYLLCVCVSSISSCIDPLIYYYASSECQRYVYSILCCKESSDPSSYNSSGQLMASKMDTCSSNLNNSIYKFLLT
hPAR2-287 KLIVTVLAMYLICFTPSNLLLVVHY FLIKSQGQSHVYALYIVALCLSTLNSCIDPFVYYFVSHDFRDHAKNALLCRSVRTVKQMQVSLTSKKHSRKSSSYSSSSTTVKTSY
```

FIG. 5B

```
Hirudin C-tail                 ..DFEEIPEEYLQ
hPAR3- 34-62 ..TLPIK / TFRGAPPN SFEEFPFSALEGWTGA..
hPAR1- 37-65 ..TLDPR / SFLLRNPNDKYEPFWEDEEKNESG..
hPAR2- 32-62 ..SSKGR / SLIGKVDGTSHVTGKGVTVETVFSVD..
```

SURFACE STAINING OF M1-epitope
+/- α-thrombin AT 37°C FOR 5 MINUTES

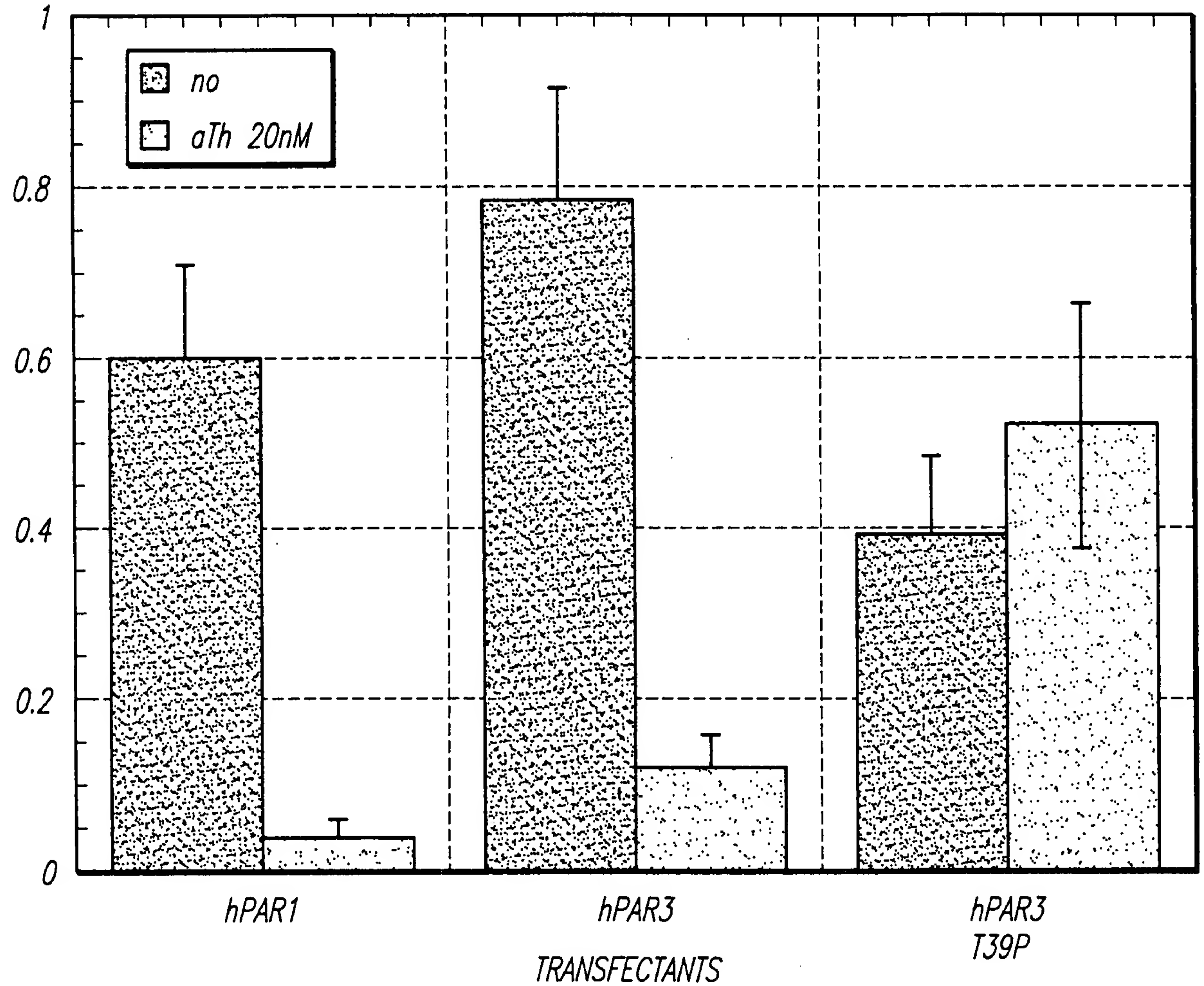


FIG. 6

FIG. 7

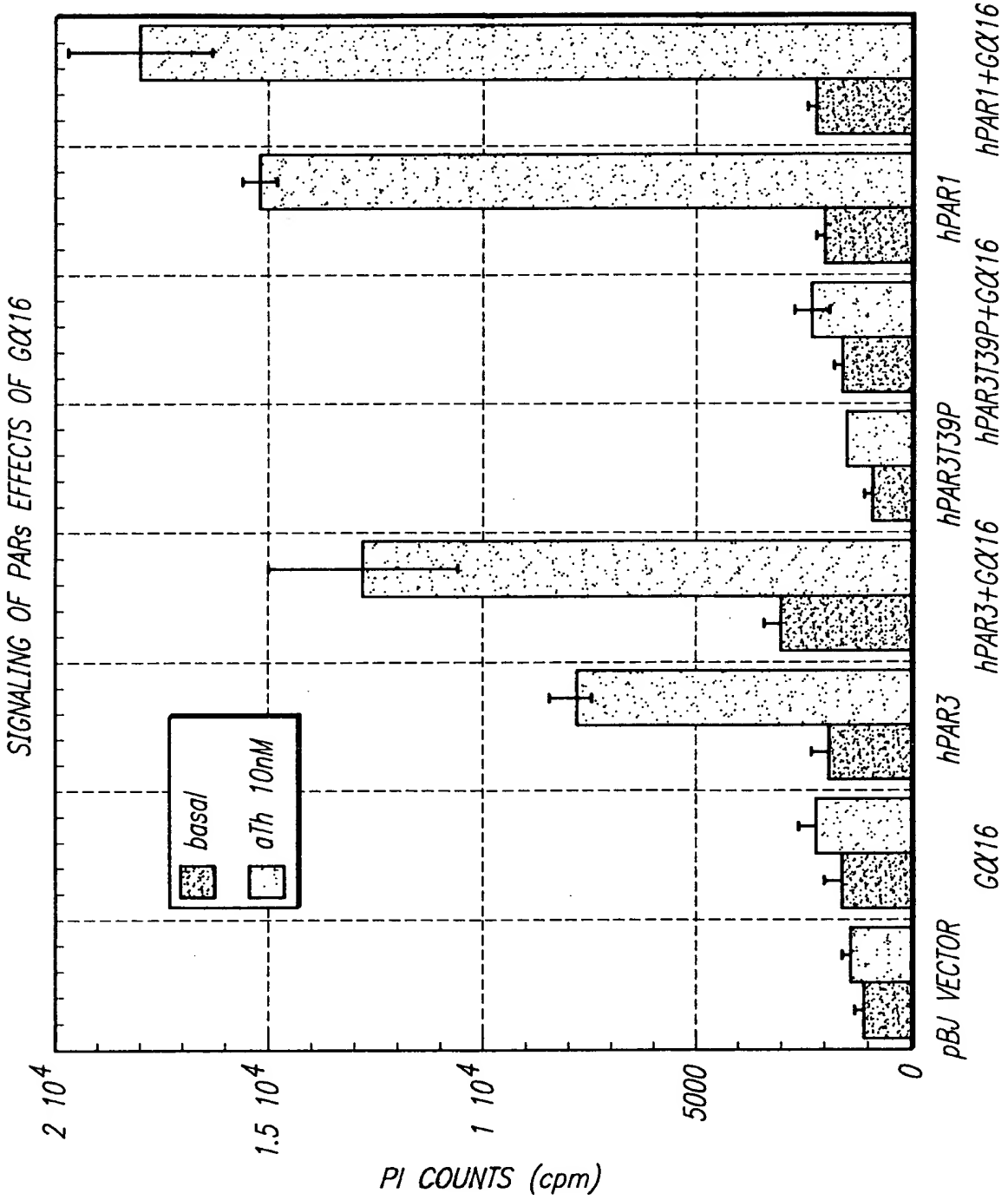

SIGNALING OF PARs EFFECTS OF Gα16
basal
aTh 10nM
PI COUNTS (cpm)
2 10^4
1.5 10^4
1 10^4
5000
0
pBJ VECTOR
Gα16
hPAR3
hPAR3+Gα16
hPAR3T39P
hPAR3T39P+Gα16
hPAR1
hPAR1+Gα16
TRANSFECTANTS

FIG. 8

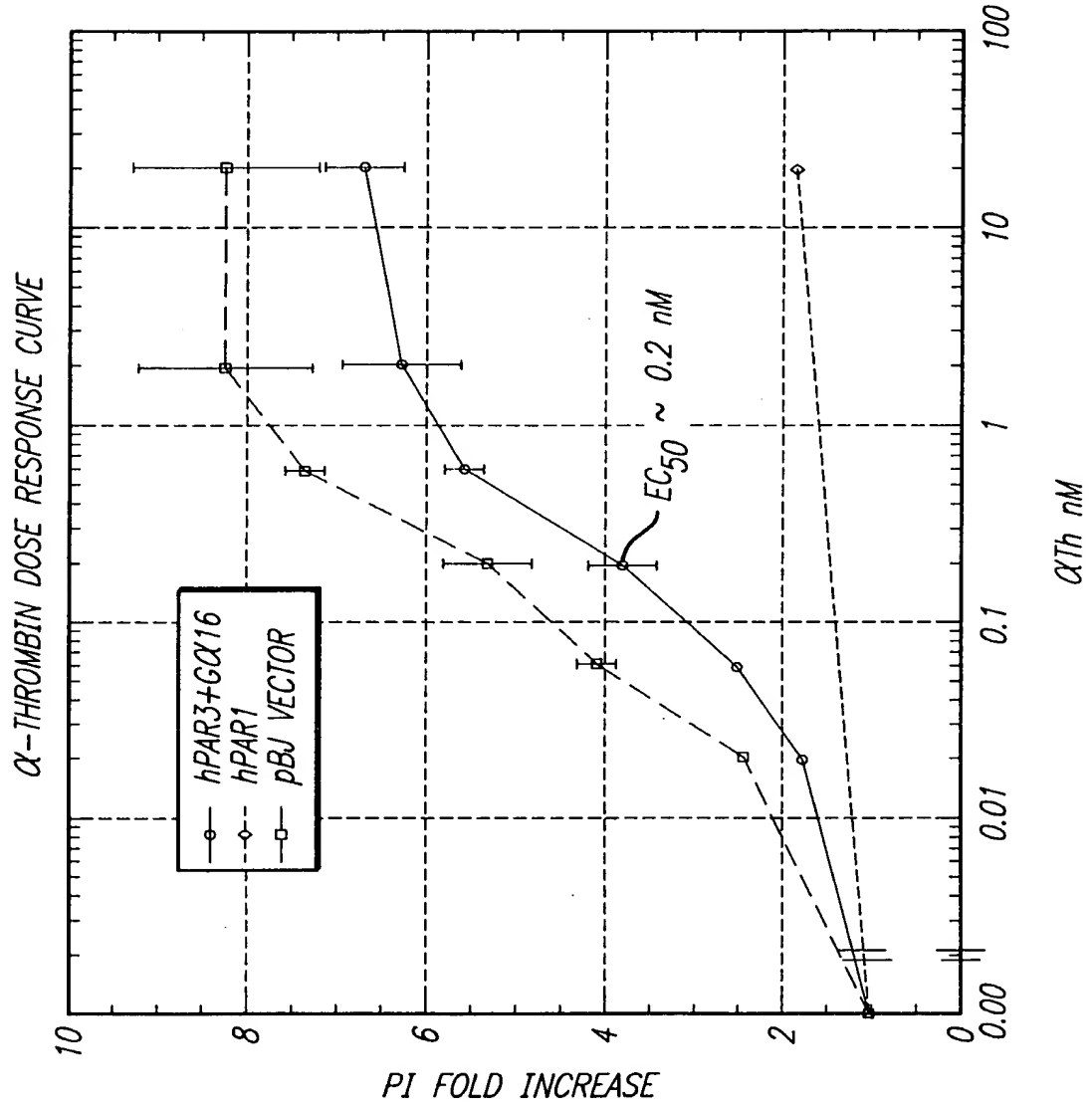
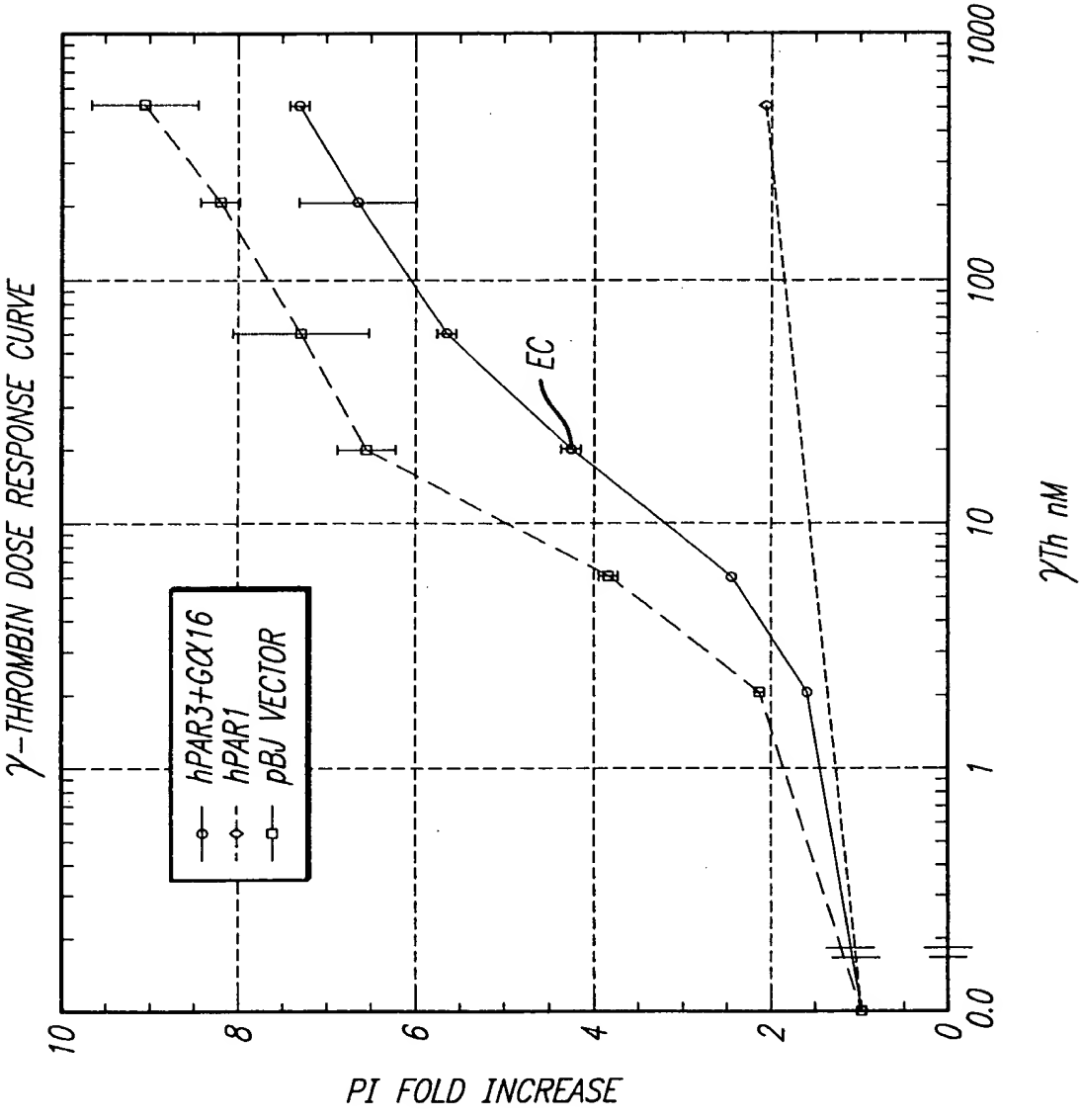

α-THROMBIN DOSE RESPONSE CURVE
hPAR3+Gα16
hPAR1
pBJ VECTOR
EC50 ~ 0.2 nM
PI FOLD INCREASE
αTh nM
0
2
4
6
8
10
0.00
0.01
0.1
1
10
100

FIG. 9


γ-THROMBIN DOSE RESPONSE CURVE
hPAR3+Gα16
hPAR1
pBJ VECTOR
EC
PI FOLD INCREASE
γTh nM
0
2
4
6
8
10
0.0
1
10
100
1000

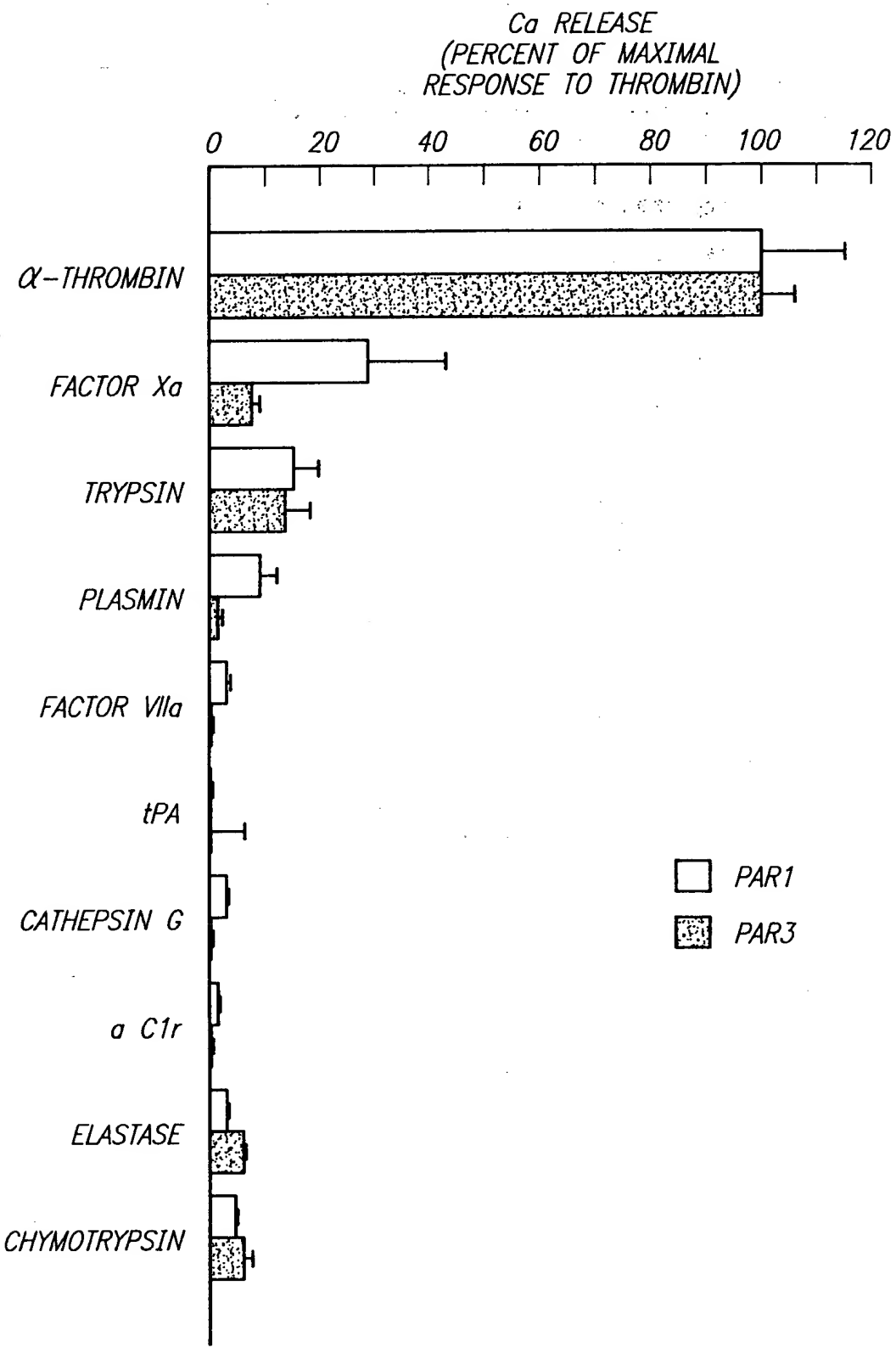

Ca RELEASE
(PERCENT OF MAXIMAL
RESPONSE TO THROMBIN)
0
20
40
60
80
100
120
α-THROMBIN
FACTOR Xa
TRYPSIN
PLASMIN
FACTOR VIIa
tPA
CATHEPSIN G
a C1r
ELASTASE
CHYMOTRYPSIN
PAR1
PAR3

FIG. 10